

REMARKS/ARGUMENTS

Claims 1, 3–21, 23–27, and 29 are pending in the above-captioned application.

Claims 1, 3–21, 23, 27, and 29 were rejected, while claims 24–26 were withdrawn by the Examiner. With this paper, claim 29 has been amended. No new matter was added with the amendment.

I. Election/Restrictions

Applicants confirm their election with traverse of the method of detecting binding activity without a modulator present. Applicants acknowledge that the Examiner has withdrawn claims 24–26 from further consideration as being drawn to a non-elected species. All of the remaining claims read on the elected species.

II. Priority

Applicants acknowledge that the Examiner has identified 5/25/2000 as the date for purposes of prior art concerning claims 1, 3–21, 23–27, and 29; however, Applicants are confused by the Examiner's decision. The limitation specifically called out by the Examiner was incorporated into claim 1 from Applicants' original claim 2, for which the Examiner had granted the benefit of priority for 09/579,111 (now U.S. Patent No. 6,649,358) as well as provisional applications 60/155,259; 60/176,001; 60/176,093; and 60/191,784 in his November 30, 2005, Office action.

III. Claim rejections under 35 U.S.C. § 112, second paragraph

Claim 29 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Applicants have corrected claim 29 to provide antecedent basis for the three limitations called out by the Examiner. With the above-described amendments, Applicants respectfully assert that claim 29 should be found to comply with the requirements of 35 U.S.C. § 112, second paragraph.

The Examiner states on page 6 of the current Office action, "In contrast to applicant's remarks, see p 7 (9/13/2006), it is noted that amended claim 29 does not incorporate

all the limitations of current claim 1 (i.e. ‘detecting a detectable signal …’).” There was no reason for claim 1 to include the limitation called out by the Examiner. The Examiner stated on page 10 of the May 19, 2006, Office action that claims 2, 4–12, 16, 17, 22, and 24–26 were objected to as being dependent upon a rejected base claim but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claim 1, the base claim, did not *at that time* include the limitation called out by the Examiner in the current Office action. Claim 1 was amended in Applicants’ previous paper to incorporate claim 2, which included the limitation called out by the Examiner. Claim 22 was indicated by the Examiner to be allowable if rewritten to include all the limitations of the *existing* base claim and any intervening claims, of which there were none. Claim 29 represents claim 22 rewritten in independent form to include all of the limitations of base claim 1 *as it existed when the Examiner stated claim 22 would be allowable if rewritten in independent form.*

IV. Claim rejections under 35 U.S.C. § 102(b) as being anticipated by Weigl et al. (1999 *Science* 283:346–347)

Claims 1, 3, 5, 23, and 27 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Weigl et al. (1999 *Science* 283:346–347). “[F]or anticipation under 35 U.S.C. § 102, a single reference must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present.” MPEP § 706.02. “The identical invention must be shown in as complete detail as is contained in the . . . claim.” *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, USPQ2d 1913, 1920 (Fed. Cir. 1989).

With regard to claim 1, at a minimum, Weigl et al. do not teach “detecting a detectable signal that indicates a final concentration of the at least one first component or the set of first components that remains unbound after exiting from the first channel, thereby detecting the binding activity.”

Applicants request that the Examiner compare the T-sensor of Weigl et al. with the illustrative microfluidic device of Applicants’ Figure 6. As can be seen in Figure 6, detection takes place after the unbound component or set of components exits the first channel 600. This is possible because the unbound component(s) exit into a channel 608 that is connected to but

distinct from first channel **600**. Channel **608** contains detector **606**, which detects the unbound component(s). As can be seen in Figure 6, the bound complexes exit first channel **600** into a separate channel, channel **610**. This arrangement offers the advantage that labeling is unnecessary. See, for example, Applicants' specification page 28, paragraph 0103.

Weigl et al. do not teach detecting a detectable signal that indicates a final concentration of an unbound component or set of components. In column 3, on page 346, beginning at 17 lines from the bottom, Weigl et al. teach, "As interdiffusion proceeds, interaction zones are formed in which sample and reagents may bind and react. Typically an indicator changes color or fluorescence intensity upon interdiffusion and reaction with analyte molecules." Thus, Weigl et al. teach detecting a bound and reacted component rather than an unbound component or set of components.

Weigl et al. also do not teach detecting a detectable signal that indicates a final concentration of a component or set of components that remains unbound after exiting from the first channel. While Weigl et al. do not specify where within the first channel the reacted molecules are detected, Figure 1 makes clear that they are detected within the one and only channel in which binding takes place. As seen in Figure 1, this single channel ends in a waste compartment. Therefore, the only way to detect a compound after it exits the reaction channel of Weigl et al. is to detect it within the waste compartment. Nothing in Weigl et al. suggests this.

Thus, Weigl et al. do not teach every aspect of the claimed invention either explicitly or impliedly, nor do they show the identical invention claimed by Applicants in as complete detail as is contained in independent claim 1. Withdrawal of the rejection of claim 1 under § 102(b) as being anticipated by Weigl et al. is, therefore, respectfully requested.

Claims 3, 5, 23, and 27 depend directly from claim 1. Therefore, Applicants respectfully submit that these dependent claims are allowable for at least the same reasons as set forth herein with respect to claim 1. Withdrawal of the rejection of dependent claims 3, 5, 23, and 27 under § 102(b) as being anticipated by Weigl et al. is also respectfully requested.

V. Claim rejections under 35 U.S.C. § 102(a) as being anticipated by Kamholz et al. (1999 *Anal Chem* 71:5340–5347) as evidenced by Mastro et al. (1984 *PNAS* 81:3414–3418)

Claims 1, 3, 7–15, 20, 21, 23, 27, and 29 were rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Kamholz et al. (1999 *Anal Chem* 71:5340–5347) as evidenced by Mastro et al. (1984 *PNAS* 81:3414–3418).

With regard to independent claims 1 and 29, at a minimum, Kamholz et al. and Mastro et al. do not teach “detecting a detectable signal that indicates a final concentration of the at least one first component or the set of first components that remains unbound after exiting from the first channel, thereby detecting the binding activity.”

Kamholz et al. do not teach detecting a detectable signal that indicates a final concentration of an unbound component or set of components. In column 1, on page 5340, lines 7–11, Kamholz et al. teach, “In a simple form of T-sensor, the concentration of a target analyte is determined by measuring fluorescence intensity in a region where the analyte and a fluorescent indicator have interdiffused.” See also page 5343, column 2, lines 14–16, in which Kamholz et al. state, “The extent of binding for a range of AB580 and HSA concentrations was determined based on fluorescence measurements made using a fluorometer” Kamholz et al. also teach on page 5345, column 2, lines 10–12, “the measured emission intensity is the sum of fluorescence from the complex” Thus, Kamholz et al. teach detecting an analyte-indicator complex rather than an unbound component or set of components.

Kamholz et al. also do not teach detecting a detectable signal that indicates a final concentration of a component or set of components that remains unbound after exiting from the first channel. Figure 1 of Kamholz et al. indicates that detection takes place within the one and only channel in which diffusion takes place. Nothing in Kamholz et al. suggests taking measurements after the components have exited this channel.

Mastro et al. do not provide the teachings Applicants have shown above to be missing from Kamholz et al. Therefore, Kamholz et al. as evidenced by Mastro et al. do not teach every aspect of the claimed invention either explicitly or impliedly, nor do they show the identical invention claimed by Applicants in as complete detail as is contained in independent claims 1 and 29. Withdrawal of the rejection of claims 1 and 29 under § 102(a) as being anticipated by Kamholz et al. as evidenced by Mastro et al. is, therefore, respectfully requested.

Claims 3, 7–15, 20, 21, 23, and 27 depend directly from claim 1. Therefore, Applicants respectfully submit that these dependent claims are allowable for at least the same reasons as set forth herein with respect to claim 1. Withdrawal of the rejection of dependent claims 3, 7–15, 20, 21, 23, and 27 under § 102(a) as being anticipated by Kamholz et al. as evidenced by Mastro et al. is also respectfully requested.

VI. Claim rejections under 35 U.S.C. § 103(a) as being unpatentable over Weigl et al. (1999 *Science* 283:346–347) or Kamholz et al. (1999 *Anal Chem* 71:5340–5347) as evidenced by Mastro et al. (1984 *PNAS* 81:3414–3418) in view of Suzuki et al. (1999 *JBC* 274:31131–31134)

Claims 1, 3–21, 23, 27, and 29 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over either of Weigl et al. (1999 *Science* 283:346–347) or Kamholz et al. (1999 *Anal Chem* 71:5340–5347) as evidenced by Mastro et al. (1984 *PNAS* 81:3414–3418), each taken separately in view of Suzuki et al. (1999 *JBC* 274:31131–31134). The rejection of these claims is respectfully traversed.

To warrant rejection under 35 U.S.C. § 103(a), all the claim limitations must be taught or suggested by the prior art. See MPEP § 2142. As demonstrated above, the Weigl et al., Kamholz et al., and Mastro et al. references, taken singly or combined, do not teach or suggest “detecting a detectable signal that indicates a final concentration of the at least one first component or the set of first components that remains unbound after exiting from the first channel, thereby detecting the binding activity.” Therefore, these three references neither teach nor suggest all of the limitations of independent claims 1 and 29. The Examiner does not assert that Suzuki et al. provide the missing teachings, and, in fact, Suzuki et al. do not.

Therefore, claims 1 and 29 are nonobvious over the cited references alone or in combination. Claims 3–21, 23, and 27 depend directly from claim 1. Any claim depending from a nonobvious claim is also nonobvious. See MPEP § 2143.03 and *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Thus, dependent claims 3–21, 23, and 27 are nonobvious. Withdrawal of the rejection of these claims as being unpatentable over either of Weigl et al. or Kamholz et al. as evidenced by Mastro et al. (1984 *PNAS* 81:3414–3418), each taken separately in view of Suzuki et al. is, therefore, respectfully requested.

Conclusion

For the foregoing reasons, Applicants believe all the pending claims are in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned attorney.

Respectfully submitted,



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